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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
06275-0188002

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Application Number	Filed
10/665,240	September 19, 2003

First Named Inventor
Tommy Ekstrom

Art Unit	Examiner
1627	Kendra D. Carter

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record.
Registration number 34,819

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/Janis K. Fraser/
Signature

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January 10, 2011
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Tommy Ekstrom	Art Unit	: 1627
Serial No.	: 10/665,240	Examiner	: Kendra D. Carter
Filed	: September 19, 2003	Conf. No.	: 6971
Title	: NEW USE		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW
Reasons For Which Review Is Requested

The above-captioned application stands finally rejected for obviousness for reasons stated in the Final Office action dated August 20, 2010 (the "Final Office action") at pages 5 to 20. Applicant strongly disagrees with the obviousness rejections, for reasons made of record in the many Replies filed in this case, including those filed July 27, 2007 (the "7/27/07 Reply;" see pages 10 to 29 and Exhibits 1-5 attached to that Reply) and June 3, 2010 (the "6/3/10 Reply;" see pages 10-23 and Appendices A-E attached to that Reply). Some of the reasons applicant disagrees with the rejections stem from the presence of clear legal deficiencies in positions taken by the Examiner, so are appropriate for review under the Pre-Appeal Brief Conference Pilot Program. Applicants focus on five of those reasons below.

(1) The Office has improperly dismissed the evidence of teaching-away in Exhibit 1.

Along with the 7/27/07 Reply, applicant submitted a number of exhibits as evidence in support of the nonobviousness of the invention. Exhibit 1, a copy of the prior art Pulmicort Turbuhaler® budesonide product insert, is described at pages 15-18 of the 7/27/07 Reply and again at pages 12-15 of the 6/3/10 Reply as constituting a teaching-away from the presently claimed methods. In each Office action since Exhibit 1 was first submitted, the Examiner has refused to grant this evidence of teaching-away any weight at all. The Examiner dismisses the evidence as irrelevant because it concerns only budesonide, rather than a budesonide/formoterol combination product such as used in the presently claimed methods, citing a standard appropriate for evidence of surprising results, but not for evidence of a teaching-away. See, for example, the

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remarks regarding Exhibit 1 in the Office action dated March 4, 2010 at pages 14-15: "**It is noted that evidence of unexpected results is required to be reasonably commensurate in scope with the claimed invention**." Applicant has pointed out repeatedly (see, e.g., the Reply filed December 11, 2009 at pages 4-5, and the 6/3/10 Reply at pages 13-14) that Exhibit 1 was cited as a teaching away, not as surprising results, and that a teaching away reference need not include all of the limitations of the claim. (Indeed, it cannot include all of the limitations of the claim, because then it would likely be anticipatory prior art.) To illustrate the standard that the courts apply to teaching-away evidence, Applicant cited at pages 13-15 of the 6/3/10 Reply the U.S. Supreme Court case *United States v. Adams*, as well as the *Optivus Tech. v. Ion Beam Applications* and *Takeda v. Alphapharm* Federal Circuit decisions. Despite this, the Examiner persists in dismissing the teaching-away evidence of Exhibit 1, improperly arguing at page 15 of the Final Office action that

> **the evidence provided in Exhibit 1 is not a true comparison of the claimed invention because the Exhibit 1 is administration of budesonide as the sole active ingredient, while the claimed invention is an admixture of budesonide and formoterol....In order to truly compare the two compositions both compounds need to be present.** (Emphasis in original.)

Applicant asks that Exhibit 1 be given due weight for the important teaching-away it represents: i.e., the teaching that a budesonide-containing product should not be inhaled more than twice per day, never "as needed," and never altering the dose without a physician's specific instruction. These warnings in Exhibit 1 stem at least in part from the recognized dangers of overdosing on corticosteroids, as illustrated in text from Exhibit 1 quoted at page 18 of the 7/27/07 Reply and referenced in the 6/3/10 Reply at page 14. Plainly, one of skill in the art would have expected similar caveats and restrictions on use of any budesonide-containing composition, including the budesonide/formoterol combination of the present claims. Rather than address this logic, the Examiner simply dismisses Exhibit 1 because it is "not a true comparison." Applicant asks that the evidence in Exhibit 1 be given proper weight as a powerful teaching-away from the presently claimed methods, and that the Examiner address the evidence on the merits rather than dismissing it out of hand.

(2) The Office has improperly dismissed the evidence of teaching-away in Exhibit 3.

Another exhibit submitted with the 7/27/07 Reply is Exhibit 3, a "Patient's Instructions for Use" relating to the Advair Diskus® combination product containing fluticasone propionate (a glucocorticosteroid, similar to budesonide) and salmeterol xinafoate (a long-acting beta-2 agonist, similar to formoterol fumarate dihydrate). Exhibit 3 is described at pages 19-21 of the 7/27/07 Reply and in each Reply submitted after that date (see, e.g., pages 17-18 of the 6/3/10 Reply) as constituting a teaching-away from the presently claimed methods because it provides evidence that those of skill in the art understood that glucocorticosteroid-containing products in general (even those formulated as combination products) should never be inhaled on an as-needed basis. The Examiner does not challenge Applicant's view of the document. Rather, the Examiner takes the position that the evidence can be ignored merely because it concerns an admixture of two drugs different from those recited in the present claims. As with Exhibit 1 discussed above, the Examiner appears to confuse the standards for surprising results with those for a teaching away reference, saying: "**In order to truly compare the two compositions both compounds need to be present. It is noted that evidence of unexpected results is required to be reasonably commensurate in scope with the claimed invention.**" (Final Office action at page 16.) Applicant asks that the evidence in Exhibit 3 be given proper weight as a powerful teaching-away from the presently claimed methods, and that the Examiner address the evidence on the merits rather than dismissing it out of hand.

(3) The Office has improperly dismissed the surprising results in Appendix A.

The 6/3/10 Reply cited Kuna et al., designated Appendix A in the 6/3/10 Reply, as objective evidence in support of nonobviousness. As explained at pages 20-21 of the 6/3/10 Reply, Kuna et al. reports the very surprising finding that patients treated in accordance with the presently claimed methods (the so-called "SMART" group) experienced fewer asthma exacerbations than a second group treated in accordance with the Carling et al. prior art method, even though the total daily dose of budesonide and formoterol fumarate dihydrate given to the second group was higher than that given to the SMART group. Rather than address this evidence of a surprising benefit regarding exacerbations, however, the Final Office action at pages 17-18 dismisses it on the ground that, for certain other parameters, such as lung function, Kuna et al. reports similar efficacy in the two treatment arms. This suggests that the Examiner

regards surprising results to be irrelevant unless the evidence shows surprising results in each and every possible parameter. Applicant maintains that this is a fundamental misunderstanding of the concept of "surprising results" as objective evidence of nonobviousness, and degrades the concept to the point it would essentially never be applicable in any situation. Applicant asks the Examiner to meet her burden by focusing on the Kuna et al. results explicitly relied upon by Applicant as evidence of surprising results (i.e, the report of a dramatic decrease in exacerbations experienced by the SMART group of patients compared to the control group), and to explain why she believes those results were expected in view of Carling et al.'s teachings.

(4) The Office has improperly dismissed the surprising results in Appendix B.

The Final Office action similarly dismisses the evidence of surprising results reported in another publication, Rabe et al., attached as Appendix B to the 6/3/10 Reply. As discussed in detail in the 6/3/10 Reply at pages 21-22, Rabe et al. discloses another clinical study comparing the treatment method of the invention to alternative treatments. Again, the presently claimed method was found to result in significantly fewer asthma exacerbations than did the alternative methods tested. And again, the Examiner dismisses these surprising results for reasons that are not based in the law: this time "**because Kuna et al. also teaches that all treatments were well tolerated**." See the Final Office action at page 18. Even if the Examiner meant to refer to Rabe et al. in that statement, Applicant fails to see the pertinence of it. Being "well tolerated" merely means they didn't cause side effects, and does nothing to counter the fact that the method of the invention produced a clear and unexpected improvement over the other tested treatments.

The meaning of the next sentence of the Final Office action is not clear: "Thus, regardless if the rate of exacerbations were lowered, the Carling et al. method still treats asthma." If the Examiner is saying that a surprising lowering of the rate of exacerbations is irrelevant merely because the prior art method "treats asthma," Applicant points out that this is contrary to law. A prior art method does not have to be inoperable in order for a surprisingly better method to be patentable over it. Applicant asks that the evidence of surprising results in Rabe et al. be evaluated in accordance with US law rather than dismissed for inappropriate reasons.

(5) The Office has improperly dismissed the evidence of nonobviousness in Appendix E.

Applicant provided further objective evidence of nonobviousness in the form of laudatory comments by experts. See the D'Urzo opinion piece attached as Appendix E to the 6/3/10

Reply. As explained at pages 22-23 of the 6/3/10 Reply, D'Urzo opined that the method of the invention is "a significant paradigm shift in asthma management," "a novel strategy," and "one of the most important advances in asthma management in many years." This praise is consistent with the comments in the Barnes editorial submitted as Exhibit 5 with the 7/27/07 Reply and discussed on pages 27-28 of the 7/27/07 Reply. The Final Office action at page 19 dismisses this cogent and objective evidence of the unexpected success of the claimed method compared to the prior art Carling et al. method, on the ground that "the Carling et al. method is effective in treating asthma." This statement suggests that the Examiner does not consider the opinions of experts in the field of asthma treatment to be pertinent to the question of obviousness, at least where the prior art method is not inoperable. Applicant submits that this is a misapprehension of the law as established by the courts. See, for example, *Litton Systems, Inc. v. Honeywell, Inc.*, 87 F.3d 1559 (Fed. Cir. 1996), *remanded*, 520 U.S. 111 (1997), *aff'd in part, rev'd in part, vacated in part & remanded*, 140 F.3d 1499 (Fed. Cir. 1998).

CONCLUSION

The record in the present case shows example after example of teachings-away in the prior art, of published clinical studies revealing strikingly unexpected benefits of the claimed method, and of lavish praise by experts in the field of asthma treatment. Under established law, all of this evidence must be taken into account when determining whether the invention is obvious. Unfortunately, the Examiner has either improperly dismissed it as irrelevant or has applied an improper standard in determining how to weigh it. Applicant respectfully requests that the Office's errors described in this Request be corrected so that all of the voluminous evidence of nonobviousness of record in this case (including but not limited to what is explicitly discussed above) can be given proper consideration under the law.

Respectfully submitted,

Date: January 10, 2011

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